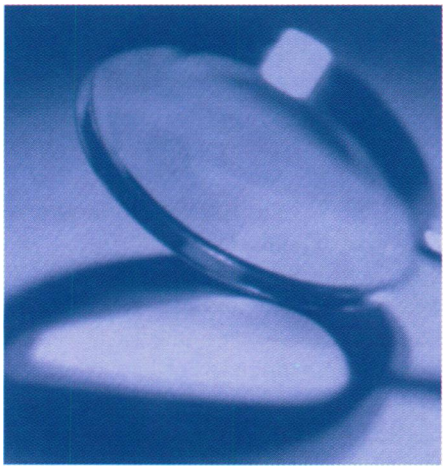

# In the Public Eye

## Media Watch

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**Medical and scientific research has become more complex and often more controversial. Local institutional review boards, regulated by the federal government, are meant to protect subjects and staff from negative consequences from participation in or proximity to research. What happens when safeguards for human or animal subjects become deficient? Who must take control to ensure safety?**

The seriousness of these questions became apparent at the end of March 1999 when, after years of investigation and advisement, the Office for Protection from Research Risk issued a directive instructing the West Los Angeles Veterans Administration to suspend federally funded human research and deactivated their "assurance" (see box). CNN and other media reported that officials at the Los Angeles veterans hospitals had allowed potentially harmful research to be carried out on patients without their proper consent. A cardiologist was accused of conducting cardiac catheterization procedures without obtaining consent. CNN quoted Republican Terry Everett, chair of the House Veterans Affairs Committee's oversight and investigations panel, as saying, "The concerns about informed consent go straight back to the awful things the Nazis did to people during the Holocaust and called it medical research. The civilized world vowed it should not happen again."

### What happened?

Initially VA researchers and the affiliated UCLA community were taken aback by the stringent ruling. To many, it seemed sudden and harsh. The letter from the Office for Protection from Research Risk, however, clearly stated that concerns over administrative deficiencies occurring over the past 6 years in the VA Greater Los Angeles Healthcare System had led to this action. The VA simply did not appear to be holding up its end of the assurance commitment. While the Office for Protection from Research Risk ordered that only federally funded human research should be stopped, another letter from Kenneth Kizer, M.D., undersecretary at the Department of Veteran Affairs, extended the suspension to animal research. Dr. Kizer also said that because West Los Angeles VA is part of a Multiple Project Human Subject Assurance, research at the entire VA Greater Los Angeles Healthcare System, including Sepulveda VA, would be suspended as a preventive rather than a punitive measure.

This suspension order meant that no new patients could be recruited and no additional animals could be purchased. Stipulations did allow existing treatments to continue if the cessation of a drug or procedure would pose a health risk to the subject. Nearly 6 years of correspondence between the Office for Protection from Research Risk and the West Los Angeles

**What is an assurance?**

An assurance with the Office for Protection from Research Risk is a formal written commitment to

1) widely held ethical principles
2) DHHS regulations for Protection of Human Subjects
3) institutional procedures adequate to safeguard the rights and welfare of human subjects.

Puglisi JT [testimony]. Subcommittee on Oversight and Investigations and Subcommittee on Health of the Committee on Veterans' Affairs (April 21, 1999).

VA document efforts by the latter to comply with the oversight agency's recommendations and provide evidence of progress. In July 1994, the Office for Protection from Research Risk placed a "restriction" on the West Los Angeles VA, requiring quarterly reports on the implementation of the recommendations, all of which had been based on Health and Human Services regulations.

### The main concerns

The investigations and recommendations centered on appropriate informed consent as well as proper approval and review of research projects. The oversight agency offered suggestions for changes in the consent language. The language was thought to be too technical for the veteran population, and it was noted that many existing consent forms omitted basic elements required by Health and Human Services. In addition, proper disclosure of information to potential research participants, in particular those with impaired decisionmaking capacity, was not sufficiently detailed. Site visits found the VA lacking consent documentation, and there was no organized filing and tracking system for consent forms.

### The role of the institutional review board

A research proposal cannot receive federal funding without approval from the institutional review board. To ascertain appropriateness and safety of a proposal, boards require a vote from a minimum of 5 people, including at least 1 scientist, 1 nonscientist, and 1 person not otherwise affiliated with the institution. To achieve a quorum, a nonscientist must be present.

Once research is approved and initiated, the institutional review board retains the responsibility of monitoring both the consent process and safety risks. The board can suspend or terminate a project if research is not being conducted in accordance with institutional review board requirements, or if it has been associated with unexpected serious risk to participants.

The Office for Protection from Research Risk reviewed minutes from 9 VA institutional research board meetings and found that 7 of those meetings lacked a quorum, rendering their decisions invalid. The office's request for board minutes to document the results of votes was also not heeded. Finally, the VA failed to secure a patient representative for the institutional review board.

AP Photo/Rich Pedroncelli

Saluting the flag during Veteran's Day ceremonies at Capitol Park in Sacramento. The public has been shocked at revelations about veterans' hospital treatment.

### The VA's response

In a letter to medical colleagues in April, Dr. Gerald S. Levey, provost of the UCLA Medical Sciences and dean of the UCLA School of Medicine, wrote that the VA Greater Los Angeles Healthcare System affiliates "have had an outstanding track record of success in both clinical and basic research, and there is need not only to preserve that success [but also] to bring the institution to an even greater level of achievement by correcting many of the administrative deficiencies that existed at the WLAVA and at Sepulveda VA."

A new acting associate chief of staff for research, Marguerite Hayes, M.D., was detailed to the site to oversee the implementation of the directives from the Office for Protection from Research Risk and VA headquarters. High on the list of her charges was the reinstitution of legally and appropriately constituted institutional review boards.

At the West Los Angeles VA alone, over 750 research projects were underway at the time the suspension was initiated. Nearly 70 were nonhuman, nonanimal, nonbiohazard studies, and those were immediately released from the suspension. As of July, all animal studies and over 90% of biohazard studies had been released. For the human studies, the 3 reconstituted institutional review boards, using proper membership representation and approval procedures, must review each protocol. Once the institutional review board approves the protocol, the Office for Protection from Research Risk and VA headquarters must grant the final authorization to resume the study. Each government-funded study must apply for a "single project assurance" (SPA).

In May, J. Thomas Puglisi, director of Human Subject Protection at the Office for Protection from Research Risk, said that few single project assurances had been received. Of the over 400 human subject studies, 14% are government-funded, through NIH or the Department of Veterans Affairs. None of these government-funded projects has been released. Most of the 13% that have been released are funded by pharmaceutical companies.

### What of the future?

Other centers are also likely to be admonished. In 1998, Rush-Presbyterian Medical Center in Chicago was given a 5-day suspension. In May 1999, Duke University was issued a letter, suspending its human research. Because Duke was under investigation for only 4 months and responded quickly with a plan to strengthen safeguards of human subjects, the government rescinded their decision only days after the suspension. The institution, however, is required to re-evaluate approximately one tenth of their studies, and the Office for Protection from Research Risk has placed a restriction on the medical center, requiring training and education for research personnel on human subject protection guidelines.

Undersecretary Kiser has established an Office for Research Compliance and Assurance within the Veterans Administration. This office will provide evidence that research is conducted in accordance to safety regulations and with ethical and scientific integrity.